

Voltage-Gated Ion Channels and the Action Potential

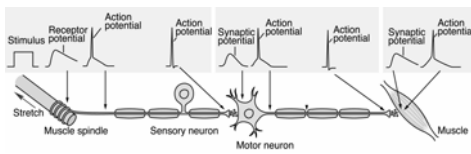
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Principles of Neural Science, chaps 8&9

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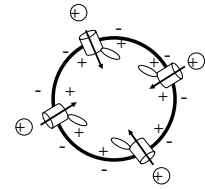
- The Action Potential
 - Generation
 - Conduction
- Voltage-Gated Ion Channels
 - Diversity
 - Evolutionary Relationships

Electrical Signaling in the Nervous System is Caused by the Opening or Closing of Ion Channels



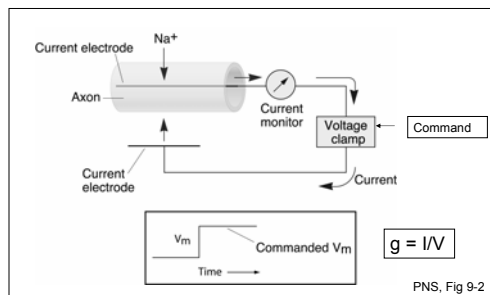
PNS, Fig 2-11

Electrical Signaling in the Nervous System is Caused by the Opening or Closing of Ion Channels



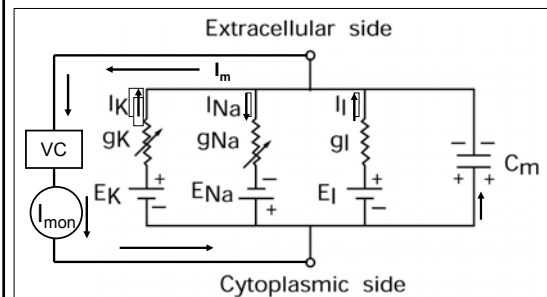
The Resultant Flow of Charge into the Cell Drives the Membrane Potential Away From its Resting Value

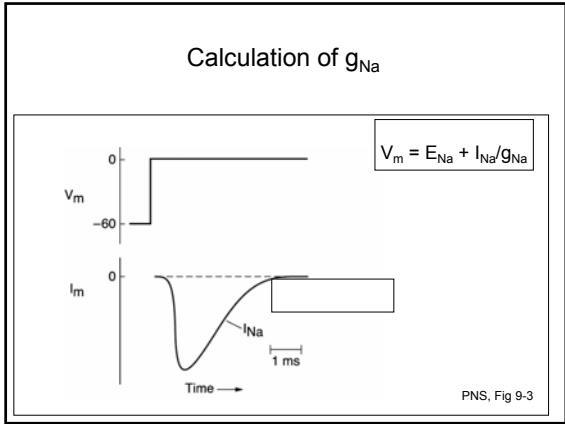
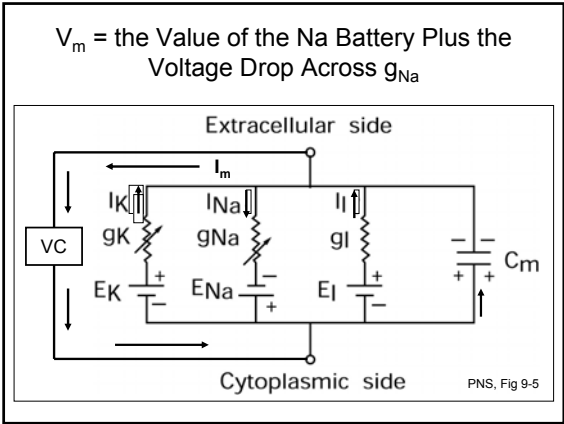
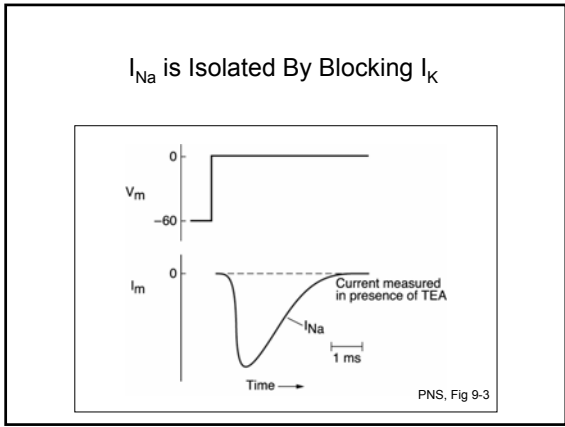
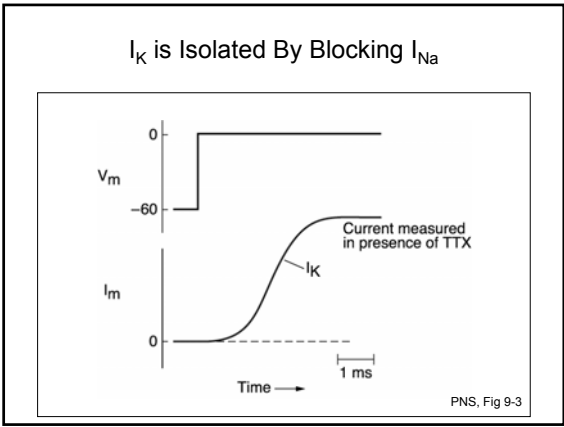
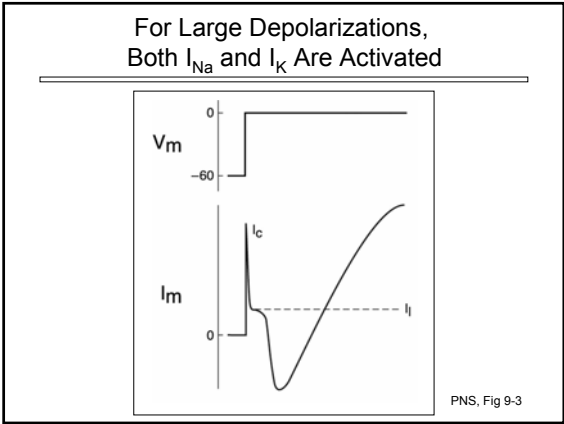
Electronically Generated Clamp Current Counterbalances the Na⁺ Membrane Current

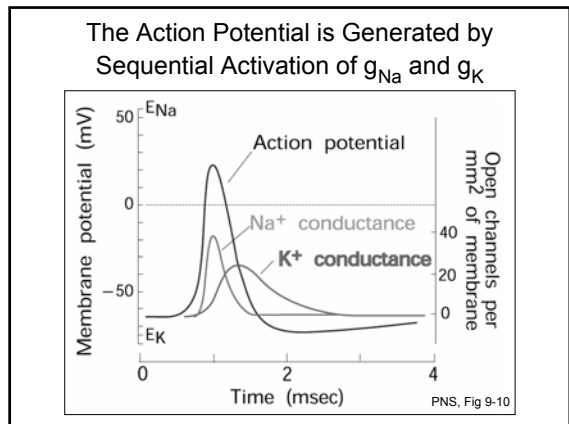
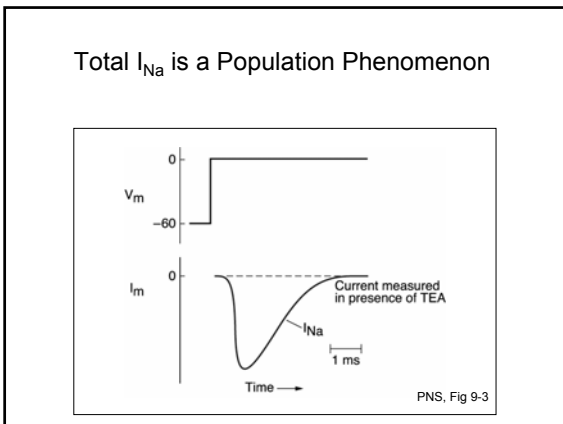
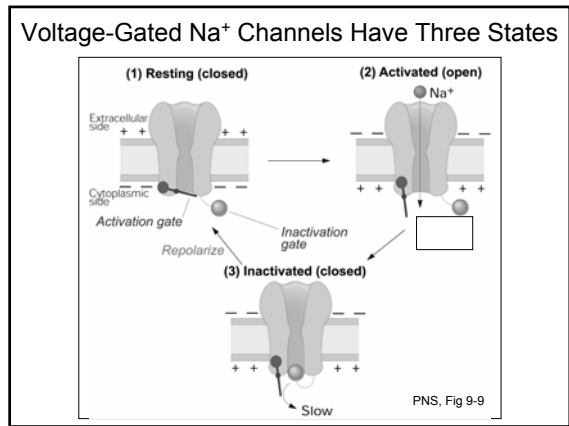
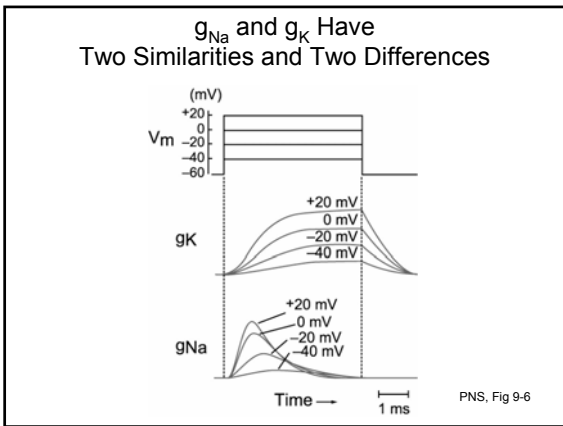
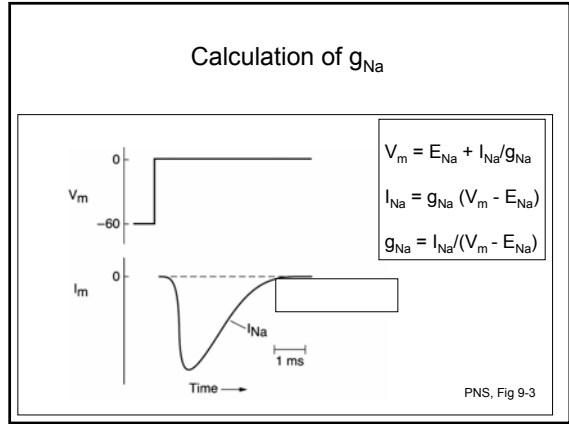
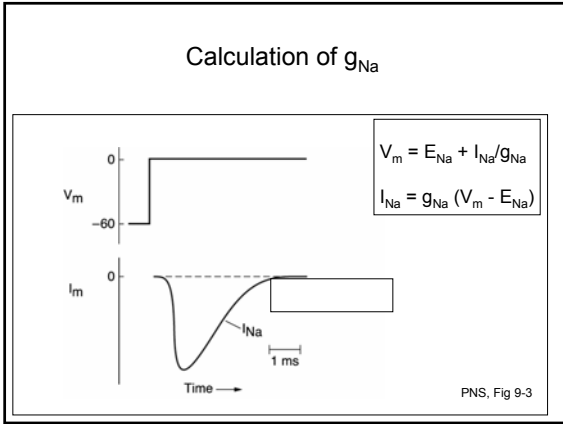


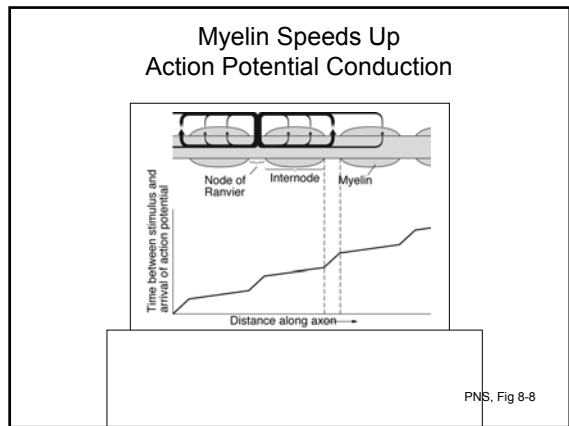
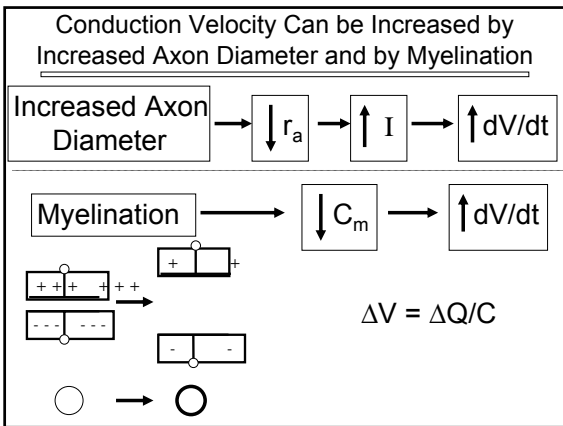
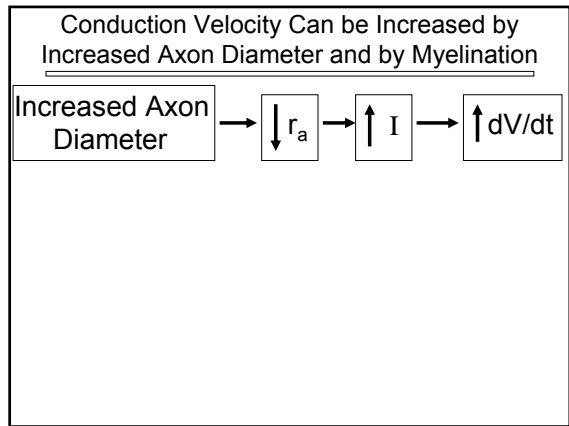
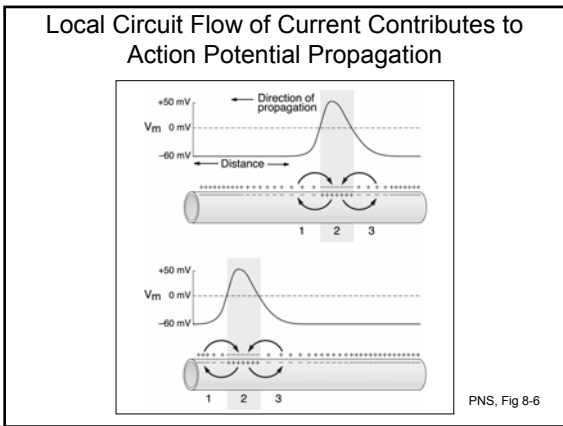
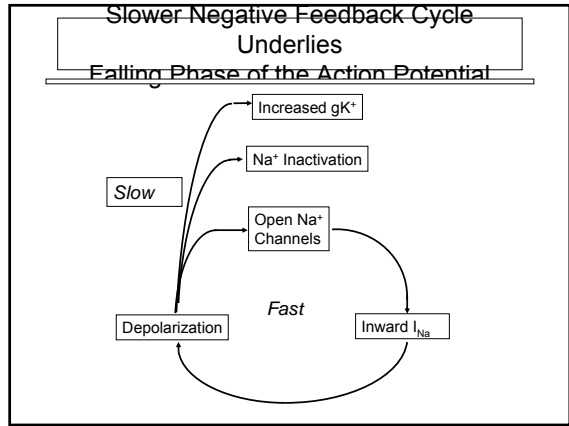
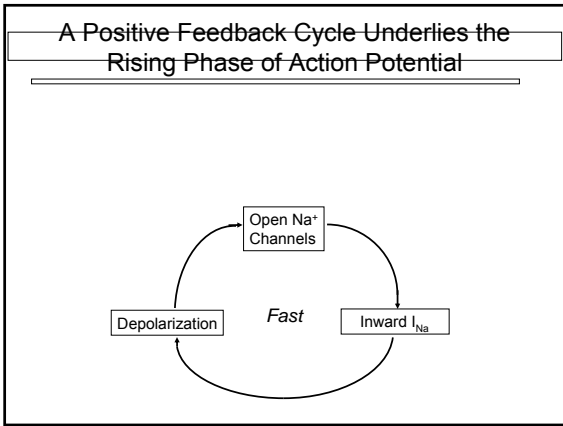
PNS, Fig 9-2

Equivalent Circuit of the Membrane Connected to the Voltage Clamp





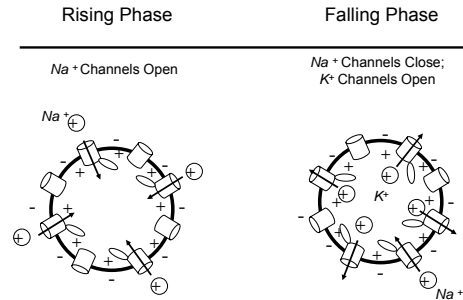




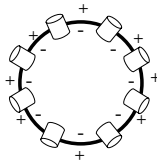
Voltage-Gated Ion Channels and the Action Potential

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Opening of Na⁺ and K⁺ Channels is Sufficient to Generate the Action Potential



However, a Typical Neuron Has Several Types of Voltage-Gated Ion Channels



Functional Properties of Voltage-Gated Ion Channels Vary Widely

- Selective permeability
- Kinetics of activation
- Voltage range of activation
- Physiological modulators

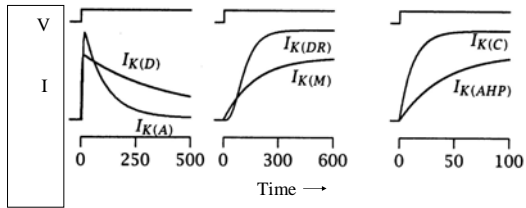
Voltage-Gated Ion Channels Differ in their Selective Permeability Properties

<u>Cation Permeable</u>	<u>Anion Permeable</u>
Na ⁺	Cl ⁻
K ⁺	
Ca ⁺⁺	
Na ⁺ , Ca ⁺⁺ , K ⁺	

Functional properties of Voltage-Gated Ion Channels Vary Widely

- Selective permeability
- Kinetics of activation
- Voltage range of activation
- Physiological modulators

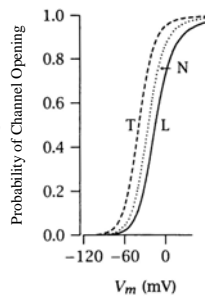
Voltage-Gated K⁺ Channels Differ Widely in Their Kinetics of Activation and Inactivation



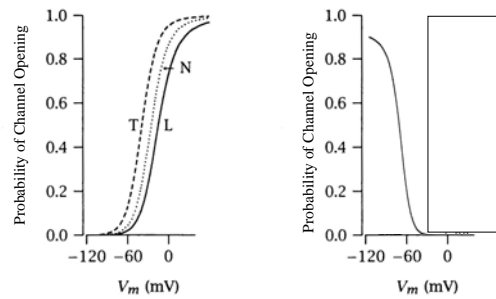
Functional properties of Voltage-Gated Ion Channels Vary Widely

- Selective permeability
- Kinetics of activation
- Voltage range of activation
- Physiological modulators

Voltage-Gated Ca⁺⁺ Channels Differ in Their Voltage Ranges of Activation



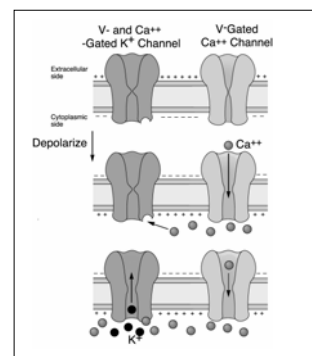
The Inward Rectifier K⁺ Channels and HCN Channels Are Activated by Hyperpolarization



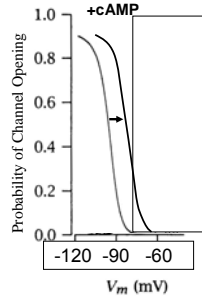
Functional properties of Voltage-Gated Ion Channels Vary Widely

- Selective permeability
- Kinetics of activation
- Voltage range of activation
- Physiological modulators: e.g., phosphorylation, binding of intracellular Ca⁺⁺ or cyclic nucleotides, etc.

Physiological Modulation



HCN Channels That Are Opened by Hyperpolarization Are Also Modulated by cAMP



Voltage-Gated Ion Channels Belong to Two Major Gene Superfamilies

- I. Cation Permeant
- II. Anion Permeant

Voltage-Gated Ion Channel Gene Superfamilies

I) Channels With Quaternary Structure Related to Voltage-Gated, Cation-Permeant Channels:

A) Voltage-gated:

- K⁺ permeant
- Na⁺ permeant
- Ca²⁺ permeant
- Cation non-specific permeant

Voltage-Gated Ion Channel Gene Superfamily

I) Channels With Quaternary Structure Related to Voltage-Gated, Cation-Permeant Channels:

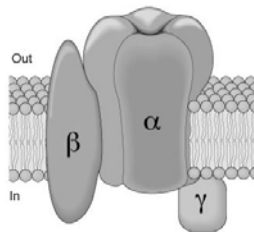
A) Voltage-gated:

- K⁺ permeant
- Na⁺ permeant
- Ca²⁺ permeant
- Cation non-specific permeant (HCN)

Structurally related to-

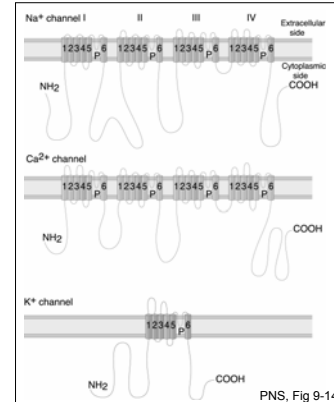
- B) Cyclic Nucleotide-Gated (Cation non-specific permeant)
- C) K⁺-permeant leakage channels
- D) TRP Family (cation non-specific); Gated by various stimuli, such as osmolarity, pH, mechanical force (Stretch or sound), ligand-binding and temperature

The α -Subunits of Voltage-Gated Channels Have Been Cloned

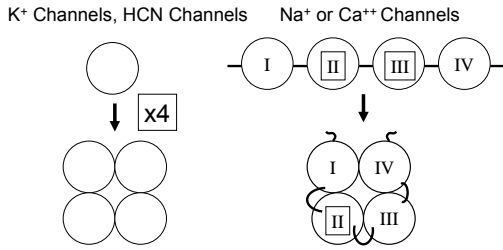


PNS, Fig 6-9

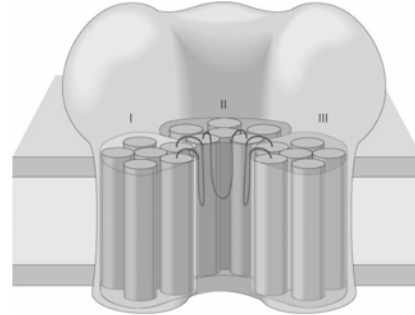
Voltage-Gated Cation-Permeant Channels Have a Basic Common Structural Motif That is Repeated Four-fold



Four-Fold Symmetry of Voltage-Gated Channels Arises in Two Ways

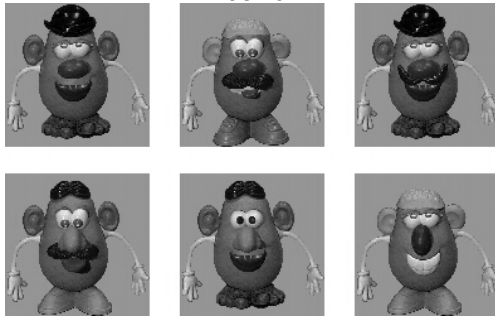


P-Loops Form the Selectivity Filter of Voltage-Gated Cation-Permeant Channels

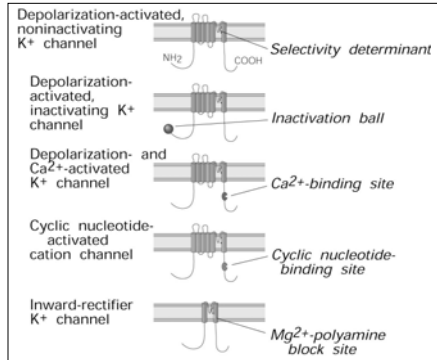


PNS, Fig 9-15

Ion Channels Evolve in a Modular Fashion



Modular Construction of K⁺ Channels



Voltage-Gated Ion Channel Gene Superfamilies

II) "CLC" Family of Cl⁻-Permeant Channels (dimeric structure):

- Gated by:
- Voltage - particularly important in skeletal muscle
 - Cell Swelling
 - pH

Voltage-Gated Cl⁻ Channels Are Dimers They Differ in Sequence and Structure from Cation-Permeant Channels

